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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/046,491	10/29/2001	Steven L. Wechsler	18810-82002	6806

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EXAMINER

WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/046,491

Applicant(s)

WECHSLER ET AL.

Examiner

Anne Marie S. Wehbe

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 April 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 185-210 is/are pending in the application.
- 4a) Of the above claim(s) 203-207 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 201 and 208-210 is/are allowed.
- 6) ☒ Claim(s) 185-187, 189-191, 193-200 and 202 is/are rejected.
- 7) ☒ Claim(s) 188 and 192 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendment and response received on 3/12/04 has been entered. New claims 203-210 have been added. Claims 185-210 are currently pending in the instant application. Newly submitted claims 203-207 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 203-207 are drawn to non-human mammals. The original claims examined in the office action mailed on 9/25/03 were directed to HSV-1 derived vectors, and mammalian cells comprising said vectors. While the previous office action did raise the issue in regards to claims 195-200, drawn to mammalian cells, as to whether the applicant intended these claims to read on cells present in a mammal, the original claims were drawn to the cell product and not to a non-human mammal comprising the cell. The cell comprising the HSV vector is patentably distinct from a non-human mammal comprising said cell in that the two products are used for substantially different purposes are made using substantially different techniques and reagents, and have different structural, physical, and functional properties. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 203-207 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP 821.03. Claims 185-202 and 208-210 are currently under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Oath/Declaration

The office acknowledges the receipt on 3/12/04 of the supplemental declaration with includes the citizenship of inventor Anthony B. Nesburn.

Claim Rejections - 35 USC 101

The rejection of claims 195-200 under 35 U.S.C. 101 for claiming non-statutory subject matter is withdrawn in view of applicant's amendments to the claims.

Claim Rejections - 35 USC 112

The rejection of claims 195-200 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicant's amendments to the claims.

Claim Rejections - 35 USC 103

The rejection of claims 185-187, 189, 195-197, 198-200, and 202 under 35 U.S.C. 103(a) as being unpatentable over U.S. 6,193,980 B1 (2/27/01), hereafter referred to as

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Efstathiou et al. in view of U.S. Patent No. 6,340,672 B1 (1/22/02), hereafter referred to as Roizman et al., is maintained. Applicant's amendments to the claims and arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection.

The applicant has amended the claims to recite an HSV-1 derived vector comprising DNA having at least one functional LAT promoter and further having a deletion in both copies of the HSV-1 LAT gene structural region, and a deletion in both copies of the HSV-1 ICP34.5 gene such that functional RNA transcripts encoding the LAT gene product and the ICP34.5 gene product cannot be detected in a cell hosting the vector, *wherein the HSV-1 derived vector does not reactivate from latency.*

The applicant argues that neither of the single null mutant HSV-1 derived vectors taught by Efstathiou and Roizman have this property, and that neither of Efstathiou et al. or Roizman et al. teach or suggest that a double null mutant of LAT and ICP 34.5 would not reactivate from latency. In support of this argument, the applicant quotes from pages 3-4 of the instant specification which state that the spontaneous reactivation rates of ICP 34.5 mutants is not entirely eliminated, citing papers by Perng et al. (see the applicant's response page 10, and the specification at pages 3-4). However, the Perng et al. papers cited by the specification are both directed to a specific HSV mutant *d*34.5 which is different from the R3616 mutant disclosed by Roizman et al. in the '672 patent cited in this rejection. Since Roizman et al. teaches that the ICP34.5 mutant viruses such as R3616 cannot replicate and spread, see columns 5-6, bridging sentence, the spontaneous reactivation observed by Perng et al. appears to be specific to the *d*34.5 strain. Therefore, since Roizman et al. teaches that HSV ICP 34.5

strains such as the R3616 strain are incapable of replication and spread, the skilled artisan would have had a reasonable expectation that mutant viruses based on the R3616 strain would also be incapable of replication and spread.

The applicant further argues that there is no suggestion in either Efstathiou or Roizman to combine the single HSV null mutants taught by each reference to generate a double null mutant HSV according to the instant claims. In response, it appears that Applicants are arguing that the cited references do not expressly suggest the claimed invention. However, it is well established in case law that a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests. *In re Burkel*, 201 USPQ 67 (CCPA 1979). Furthermore, in the determination of obviousness, the state of the art as well as the level of skill of those in the art are important factors to be considered. The teaching of the cited references must be viewed in light of these factors. It is further noted, that the test for combining references is not what the individual references themselves suggest, but rather what the combination of disclosures taken as a whole would have suggested to one of ordinary skill in the art. *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). For the purpose of combining references, those references need not explicitly suggest combining teachings, much less specific references. *In re Nilssen*, 7 USPQ2d 1500 (Fed. Cir. 1988). In the instant case, Efstathiou et al. teaches recombinant HSV-1 vectors and viruses in which an heterologous DNA is operatively linked to the LAT promoter, thus introducing a deletion into the LAT region such that normal LAT transcripts are not detected (Efstathiou et al., Figure 5, columns 3-4 and columns 13-14). Efstathiou et al. also teaches that recombinant HSV vectors and viruses with a deletion in the LAT region can also lack functional forms of various HSV

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regulatory proteins, and can be replication defective and/or attenuated (Efstathiou et al., column 6). Roizman et al. supplements Efstathiou by teaching that the R3616 virus ranks among the least pathogenic and most attenuated viruses at the time of filing (Roizman et al., column 17, lines 22-24). Therefore, based on the suggestion by Efstathiou et al. to use HSV vectors encoding a heterologous gene operatively linked to the LAT promoter that are replication defective and/or attenuated due to additional mutations in other regulatory proteins, and the teachings of Roizman et al. that an HSV virus having a deletion in both copies of the ICP 34.5 gene is among the least pathogenic and most attenuated of known HSV viruses, it would have been *prima facie* obvious to the skilled artisan to introduce the heterologous gene into the LAT region of the R3616 virus in order to generate an HSV which is capable of expressing the heterologous protein for extended periods of time, and which is has decreased neurovirulence. Further, as noted in the preceding paragraph, since Roizman et al. teaches that the ICP 34.5 mutant vectors such as R3616 described in the patent are incapable of replication and spread, the skilled artisan would have had a reasonable expectation that mutant viruses based on the R3616 strain would also incapable of replication and spread. Note that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. ' 103, all that is required is a reasonable expectation of success. See *In re O'Farrell*, 7 USPQ2d 1673 (CAFC 1988).

The rejection of claims 190-191, and 193-194 under 35 U.S.C. 103(a) as being unpatentable over U.S. 6,193,980 B1 (2/27/01), hereafter referred to as Efstathiou et al. in view of U.S. Patent No. 6,340,672 B1 (1/22/02), hereafter referred to as Roizman et al., as

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applied to claims 185-187, 189, 195-197, 198-200, and 202 above, and further in view of WO 9804726 (2/5/98), hereafter referred to as Coffin et al., is maintained. Applicant's amendments to the claims and arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection.

Applicant's arguments are they pertain to the teachings of Efstathiou et al. and Roizman et al. have been addressed in detail above and have not been found persuasive. The applicant has not provided any additional arguments regarding the teachings of Coffin et al. Therefore, the rejection of record stands.

The rejection of claim 191 under 35 U.S.C. 103(a) as being unpatentable over U.S. 6,193,980 B1 (2/27/01), hereafter referred to as Efstathiou et al. in view of U.S. Patent No. 6,340,672 B1 (1/22/02), hereafter referred to as Roizman et al., as applied to claims 185-187, 189, 195-197, 198-200, and 202 above, and further in view of Ho et al. (1996) Mol. Brain. Res., Vol. 41 (1-2), 200-209., is maintained. Applicant's amendments to the claims and arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection.

Applicant's arguments are they pertain to the teachings of Efstathiou et al. and Roizman et al. have been addressed in detail above and have not been found persuasive. The applicant has not provided any additional arguments regarding the teachings of Ho et al. Therefore, the rejection of record stands.

Claims 188, 192, 201, and 208-210 appear to be free of the prior art of record as the prior art of record does not appear to teach or suggest the Prom Δ LAT Δ 34.5 HSV vector with or without GFP.

Claims 188 and 192 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 201, and 208-210 appear to be allowable at this time.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be

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reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. For all official communications, the technology center fax number is (703) 872-9306. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

A handwritten signature in cursive script, appearing to read 'Anne M. Wehbe', written in black ink.